201-14888

COURTNEY M. PRICE
VICE PRESIDENT
CHEMSTAR

American Chemistry Council Good Chemistry Makes It Possible

December 10, 2003

By Mail
Mike Leavitt, Administrator
U.S. EPA
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program – Test Plan Submission from HERTG
Registration Number

Dear Administrator Leavitt:

The American Chemistry Council Petroleum Additives Panel (Panel) Health, Environmental, and Regulatory Task Group (HERTG) submits for review and public comment its test plan as well as related robust summaries for Phenol, heptyl derivatives (CAS #72624-02-3) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program. The HERTG understands that there will be a 120-day review period for the test plan report and that all comments generated by or provided to EPA will be forwarded to the HERTG for consideration.

Thank you in advance for your attention to this matter. If you have any questions regarding the test plan report or the robust summaries, please contact Sarah Loftus McLallen at 703-741-5614 (telephone), 703-741-6091 (telefax) or Sarah_McLallen@americanchemistry.com (e-mail).

Sincerely yours,

cc: HERTG Members

201-14888B

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For

Phenol, Heptyl Derivatives

Prepared by
The American Chemistry Council
Petroleum Additives Panel
Health, Environmental, and Regulatory Task Group

December 2003

LIST OF MEMBER COMPANIES IN THE
HEALTH, ENVIRONMENTAL AND REGULATORY TASK GROUP

The Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council Petroleum Additives Panel includes the following member companies:

Chevron Oronite Company, LLC

Crompton Corporation

Ethyl Corporation

ExxonMobil Chemical Company

Ferro Corporation

Groupe SNPE

Infineum

The Lubrizol Corporation

Rhein Chemie Corporation

Rhodia, Inc.

1.0 INTRODUCTION

In March 1999, the American Chemistry Council (formerly the Chemical Manufacturers Association) Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its participating member companies committed to address data needs for certain chemicals listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. This test plan follows up on that commitment. Specifically, this test plan sets forth how the HERTG intends to address testing information for the following substance - phenol, heptyl derivatives (CAS No.: 72624-02-3).

In preparing this test plan the following steps were undertaken:

Step 1: A review of the literature and confidential company data was conducted on the physicochemical properties, mammalian toxicity endpoints, and environmental fate and effects for phenol, heptyl derivatives, using its CAS number, CAS name, and synonyms. Searches included the following sources: MEDLINE, BIOSIS, CANCERLIT, CAPLUS, CHEMLIST, EMBASE, HSDB, RTECS, EMIC, TOXLINE, TSCATS databases as well as standard handbooks and databases (e.g., Sax, CRC Handbook on Chemicals, IUCLID, Merck Index).

Step 2: The compiled data was evaluated for adequacy in accordance with the EPA guidance documentation.

Prior to initiation of the testing proposed in this test plan, the HERTG will review any relevant data available on similar alkyl phenol test plans submitted under the HPV Challenge Program for possible inclusion of that data in this test plan.

2.0 GENERAL SUBSTANCE INFORMATION

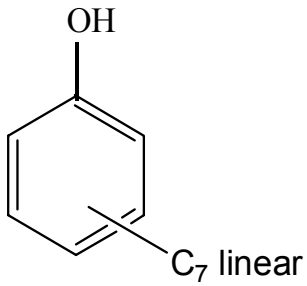
The substance that is the subject of this test plan is used as a precursor molecule in the manufacture of petroleum additives used in highly refined lubricating base oil. The chemical name, CAS Registry Number, molecular weight and chemical structure for this substance are presented below.

Chemical Name: Phenol, heptyl derivatives

Chemical Abstract Service Registry Number: 72624-02-3
Alternative Chemical Abstract Service Registry Number: 1987-50-4

Molecular Weight**:** 192.3 gm/mol

Chemical Structure:

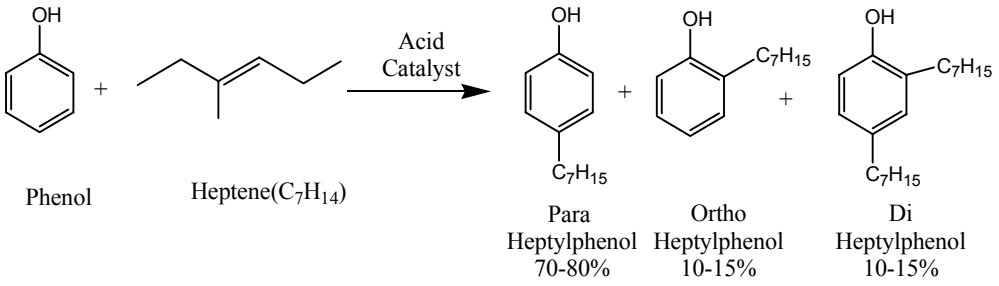


72624-02-3

3.0 EXPOSURE INFORMATION

Manufacture: Phenol, heptyl derivatives (HPL) is made through the acid-catalyzed alkylation of phenol with industrial grade heptenes. The heptenes used to make HPL are a complex mixture of branched isomers obtained from the acid catalyzed polymerization of propylene–butylene mixtures. The general reaction process is shown in Figure 1, together with the typical levels of the major components.

Figure 1



Based on supplier information, HPL has a relatively narrow homolog distribution, where C7 alkylphenol comprises greater than 95% of the total olefins in the mixture. No significant contaminates or by-products are present, and combined levels of unreacted heptene and phenol are generally less than 1% of the total mixture.

Use in Lubricants: The principal use of HPL is as a building block to manufacture higher molecular weight oligomeric lubricating additive components. These components are highly stable and not expected to release HPL under normal use in these applications. The level of unreacted HPL in these products is less than 1%.

HPL is used to manufacture a variety of lubricant additives. These additives are typically blended with other additives into lubricant concentrates, which are then sold to lubricant marketers who then blend them with oil and, in some cases, additional additives, to yield the final (finished) lubricant. This finished lubricant is then sold to the end user for use in the lubricant application.

The additives derived from HPL are used as detergents and metal deactivators in a wide variety of lubricating applications including industrial and automotive gear oils, automatic transmission formulations, and small engine applications. The average level of unreacted HPL in these finished lubricants is estimated to be very low.

4.0 PHYSICOCHEMICAL PROPERTIES

4.1 Summary of Available Data

4.1.1 Melting Point

Heptylphenol is a liquid at ambient temperature. The freezing point of heptylphenol is < -5^{o}C (Product data sheet – Schenectady International Inc.).

4.1.2 Boiling Point

The boiling point range of heptylphenol is 256 – 280^{o}C (Product data sheet – Schenectady International Inc).

4.1.3 Vapor Pressure

The vapor pressure of heptylphenol is 0.0113 mmHg @ 25^{o}C (Product data sheet – Schenectady International Inc).

4.1.4 Water Solubility

The water solubility of heptylphenol is 12.2 mg/L as measured by the shake flask method (Product data sheet – Schenectady International Inc).

4.1.5 Octanol/Water Partition Coefficient

The log octanol/water partition coefficient of heptylphenol has been estimated at 4.5 (Tollefsen et al[1].)

5.0 ENVIRONMENTAL FATE DATA

5.1 Biodegradability

5.1.1 Summary of Available Data

Phenol, heptyl derivatives are not readily biodegradable.

5.1.2 Data Assessment and Test Plan for Biodegradability

An adequate and reliable biodegradation test has been conducted on phenol, heptyl derivatives according to OECD Test Guideline 301B and ASTM D5864 guidelines using adapted inoculum. The results indicate that this material is inherently biodegradable based on a degradation of 25% after 28 days. In addition to above,

[1] Tollefsen et al. Acute Toxicity and Toxicokinetics of 4-Heptyl phenol in Juvenile Atlantic Cod (Gadus Morhua L.). Environmental Toxicology and Chemistry Vol 17, No. 4. pp. 740-746. 1998.

studies available in the literature[2] indicate approximately 40% biodegradation in seawater over 28-days. Additional biodegradation testing is not proposed.

5.2 Hydrolysis

5.2.1 Summary of Available Data

No published or unpublished hydrolysis studies with phenol, heptyl derivatives were located.

5.2.2 Data Assessment and Test Plan for Hydrolysis

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters[3] Chemically, this substance does not have hydrolysable functional groups and hydrolysis is not likely to be a significant fate process if released into the aquatic environment. Therefore, no further testing for this end point is proposed.

5.3 Photodegradation

5.3.1 Summary of Available Data

No published or unpublished photodegradation studies with phenol, heptyl derivatives were located.

5.3.2 Data Assessment and Test Plan for Photodegradation

The Atmospheric Oxidation Potential (AOP) of this substance was characterized using EPA's Quantitative Structure Activity Relationship (QSAR) program, EPIWIN[4]. Atmospheric photooxidation is the degradation of a chemical in air due to reaction with ozone or hydroxyl radicals and is dependent on the chemical structure, concentration and hydroxyl radical concentration. An overall hydroxyl rate constant of 48.8×10^{-12} cm^3/molecule-sec was calculated with a half-life of 2.6 hours. This indicates that atmospheric heptylphenol will be rapidly degraded and will not be persistent.

5.4 Fugacity Modeling

5.4.1 Summary of Available Data

No published or unpublished fugacity-based multimedia fate modeling data for phenol, heptyl derivatives was located.

5.4.2 Test Plan for Fugacity

---

[2] Brendshag, et al. Toxicity Testing and chemical characterization of produced water – A preliminary study In Ray JP, Engelhart FR Eds. Produced Water. Technological/Environmental Issues and Solutions. Plenum. New York, NY, USA. Pp 245-260.

[3] Neely, W. B. 1985. Hydrolysis. In: W. B. Neely and G. E. Blau, Eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.

[4] Estimation Program Interface for Windows (EPIWIN), Version 3.02. Syracuse Research Corporation, Syracuse, NY.

The relative distribution of phenol, heptyl derivatives among environmental compartments was evaluated using Level I Equilibrium Criterion (EQC) model[5]. Fugacity modeling was conducted using experimentally derived physico-chemical input parameters for vapor pressure, water solubility and octanol-water partition coefficient. The level I model predicts the equilibrium distribution of a fixed quantity of a chemical in a closed environment at equilibrium, with no degrading reaction, advective processes and no intermedia transport. The medium receiving the emission is unimportant because the chemical is assumed to be instantaneously distributed to an equilibrium condition. A Level III fugacity modeling is not appropriate as potential discharge rates into various environmental compartments and the reaction half-life estimates are not known for this chemical.

The Level I modeling results are presented below which indicate the likely environmental compartment into which a chemical will tend to partition and an indication of the distribution in each medium.

Chemical	Air (%)	Water (%)	Soil (%)	Sediment (%)	Sesp. Sediment (%)	Fish (%)
Heptyl Phenol	13.9	2.9	81.4	1.8	0.06	0.0046

6.0 ECOTOXICOLOGY DATA

6.1 Aquatic Toxicity

6.1.1 Summary of Available Data

Heptyl phenol is toxic to fish based on data available in the scientific literature[1]. No data was located for invertebrates or algae.

6.1.2 Data Assessment and Test Plan for Acute Aquatic Ecotoxicity

A 96-hour median lethal concentration of 0.56 mg/L was obtained in a flow through acute toxicity study conducted with juvenile fish, Atlantic cod (*Gadus morhua L.*) Aquatic toxicity testing will be conducted in invertebrates and algae according to OECD Test Guidelines 201 and 202 (Part 1).

7.0 MAMMALIAN TOXICOLOGY DATA

7.1 Acute Mammalian Toxicity

7.1.2 Summary of Available Data

Acute oral and dermal toxicity studies are available for phenol, heptyl derivatives. In these studies, the LD_{50}s are between 0.2g/kg and 2.0g/kg, respectively.

7.1.3 Data Assessment and Test Plan for Acute Mammalian Toxicity

[5] Mackay, D.A et al. Assessing the Fate of New and Existing Chemicals: A Five-Stage Process. Environ. Toxicol. Chem. 15, 1618-1626 (1996).

Adequate and reliable acute oral and dermal toxicity tests were performed for phenol, heptyl derivatives. Additional acute mammalian toxicity testing will not be conducted.

7.2. Mutagenicity

7.2.1 Summary of Mutagenicity Data

An adequate and reliable gene mutation study was performed for phenol, heptyl derivatives. The test substance was not mutagenic in the assay with or without metabolic activation.

7.2.2 Data Assessment and Test Plan for Mutagenicity Toxicity

A chromosomal aberration study will be conducted according to OECD Test Guideline 473.

7.3 Repeated-dose, Reproductive and Developmental Toxicity

7.3.1 Summary of Repeated-Dose Toxicity Data

No published or unpublished repeat dose, reproductive or developmental toxicity tests for phenol, heptyl derivatives were located.

7.3.2 Data Assessment and Test Plan for Repeated-dose Toxicity

A combined repeated dose toxicity study with a reproduction/developmental toxicity-screening test will be conducted according to OECD Test Guideline 422.

8.0 SUMMARY

The following table summarizes the proposed testing on phenol, heptyl derivatives.

Table 1
Summary Table of Available Data and Proposed Testing on
Phenol, Heptyl Derivatives

CAS No.: 72624-02-3	Study Results	Testing Proposed
Physical/Chemical Characteristics		
Melting Point	Not Applicable	No
Boiling Point	256 - 280°C	No
Vapor Pressure	0.0113 mm Hg @ 25ºC	No
Water Solubility	12.2 mg/L	No
Partition Coefficient	4.5 experimental	No
Environmental Fate		
Biodegradation	Inherently biodegradable (25% in 28 days)	No
Hydrolysis	Technical discussion included	No
Photodegradation	Modeling results included	No
Fugacity	Modeling results included	No
Ecotoxicity		
Acute Toxicity to Fish	96 hour LC50 = 2.9umol/L	No
Acute Toxicity to Invertebrates	No Data Located	Yes
Acute Toxicity to Algae	No Data Located	Yes
Mammalian Toxicity		
Acute Toxicity	Oral LD_{50} > 0.2 g/kg (rat) Dermal LD_{50} >2.0 g/kg (rabbit)	No
Repeated Dose Toxicity	No Data Located	Yes
Developmental Toxicity	No Data Located	Yes
Reproductive Toxicity	No Data Located	Yes
Genotoxicity		
Gene Mutation	Not Mutagenic	No
Chromosomal Aberration	No Data Located	Yes

201-14888B

Substance Group: **Phenol, Heptyl Derivatives**

Summary prepared by: **Petroleum Additives Panel**
Health & Environmental Research Task Group

Date: **December 2003**

1. Physicochemical properties

1.0 Octanol/Water Partition Coefficient

Robust Summary 28-Octanol-1

CAS No.	72624-02-3
Test Substance Name	Phenol, heptyl derivatives
Method/Guideline	n-Octanol/Water Partition Coefficient, OECD Method 117
GLP (Y/N)	*Not Specified*
Year (Published)	1998
Remarks for Test Conditions	Method involved high performance liquid chromatographic (HPLC) correlation analysis using a reverse phase column. The mobile phase consisted of 70% methanol/30% distilled water with a flow of 1 mL/minute at ambient temperature. Reference materials included: 2-ethylphenol, 2-npropylphenol, naphthalene, biphenyl, phenanthrene and fluoranthenc. The reference and test material were dissolved in methanol (0.1-0.3 mg/mL) and duplicate (5 uL) aliquots were applied to the column. The effluent was monitored at 254 and 270 nm. All reference materials and the test substance had a purity of at least 97%. A calibration curve was prepared on the basis of published K_{ow} values for the reference materials and their retention in the HPLC column, expressed as the capacity factor (k) according to the OECD Guideline.
Results	The HPLC correlation analysis revealed that the test material is moderately hydrophobic with a log K_{ow} of 4.5.
Conclusions	The n-octanol/water partition coefficient (log K_{ow}) was 4.5.
Data Quality	Reliable without restriction (Klimisch Code)
References	Environmental Toxicology and Chemistry, Volume 17, No. 4, 740-746 (1998).
Prepared	September 5, 2003

2. Environmental Fate and Pathways

2.0 Biodegradation

Robust Summary 28-Biodeg-1

Test Substance	
CAS #	CAS# 72624-02-3
Chemical Name	Phenol, heptyl derivatives
Remarks	100% active ingredient
Method	
Method/Guideline Followed	OECD 301B, Ready Biodegradability, Modified Sturm Test; ASTM D 5864-95
Test Type (aerobic/anaerobic)	Aerobic
GLP (Y/N)	Y
Year (study performed)	1997
Contact time (units)	28 days
Test apparatus	*Glass 4-liter Erlenmeyer flasks*
Inoculum	Activated sewage sludge from a domestic wastewater treatment plant prepared with soil filtrate per test guideline. Three cultures/group were prepared. The final combined volume of test medium, test substance and inoculum in each test container was 3 liters. Solutions were continuously aerated with CO_2 free air. The test substance was incrementally added at concentrations of 4, 8 and 8 mg C/L on days 0, 7 and 11. On day 14 equal volumes of each culture were combined and the composite inoculum screened and homogenized. A standard plate count was performed on the inoculum. Plates were incubated at 20±3°C for approximately 48 hours.
Cultures/replicates:	*Three replicate test cultures, three replicate blank control cultures and three reference control cultures.*
Temperature of incubation:	20±3°C
Dosing procedure:	Neat test chemical was gravimetrically added to glass cover slips, which were then added to culture medium in test vessels.
Study initiation:	Test flasks provided with CO_2 free air and mixed with a magnetic stirrer. The CO_2 produced from the degradation of organic carbon sources within each test chamber was trapped as K_2CO_3 in 0.5 N KOH and measured using a carbon analyzer.
Sampling:	Days 2, 5, 11, 13, 16, 18, 23 and 29 (after acidification on day 28)
Concentration of test substance:	10 mg C/L weighed directly onto tared glass slides and placed into each test substance flask.
Controls:	Blank and positive controls used per guideline. Positive control was canola oil added to control vessels at a loading of 10 mg C/L.
Analytical method:	The CO_2 produced from the degradation of organic carbon sources within each test chamber was trapped as K_2CO_3 in 0.5 N KOH and measured using a carbon analyzer.

Study termination:	On day 28 the pH of the content of each test flask was determined. The flasks were then acidified with 3 ml of concentrated hydrochloric acid to drive off inorganic carbonate. The chambers were aerated overnight and then the trapping solutions closest to the test chambers were analyzed for inorganic carbon.
Method of calculating biodegradation values:	Percent biodegradation calculated as percent ratio of cumulative net carbon dioxide to theoretical carbon dioxide as determined from elemental analysis of the test material.
Results	The test substance was not considered readily biodegradable under the criteria that requires 60% biodegradation within 28 days, achieved within 10 days of reaching 10% biodegradation. The CO_2 production from the reference chemical exceeded the 60% of theoretical necessary to consider the test valid.
Degradation %	Test substance: 25.4 $\pm$ 1.4 % in 29days (average final pH 7.1) Positive control substance: 91.5 $\pm$ 0.8 % in 29 days
Conclusions	The test substance was not readily biodegradable.
Data Quality	Reliable without restriction. (Klimisch Code)
References	Confidential business information
Other	Updated: 5/27/2003

AQUATIC ORGANISMS

3.0 Acute and Prolonged Toxicity to Fish

Robust Summary 28-Fish-1

Test Substance	
CAS #	CAS# 72624-02-3
Chemical Name	Phenol, heptyl derivatives
Remarks	Minimum of 97%
Method	
Method/Guideline followed	Similar to OECD Guideline for Testing of Chemicals #203, Fish Acute Toxicity Test (1984).
Test Type	Acute Toxicity to Fish (flow through test conditions)
GLP (Y/N)	Not specified
Year (Study Published)	1998
Species/Strain	Atlantic Cod
Fish Number	21/concentration (7/replicate)
Fish Size	Average weight 1.1 g
Analytical Monitoring	Not specified
Nominal Test Substance Concentration Levels	Vehicle Control (methanol treated water), 0.5, 1, 2.1 and 4.2 umol/L
Test Concentration Preparation	Not Described
Exposure Period	168 hours
Exposure Conditions	Flow through test conditions.
Vehicle	Methanol
Statistical Analysis	ANOVA, Mann-Whitney U test
Dose Rangefinding Study	No
Test Chambers	1.5-liter glass aquaria
Diluent Water	Temperature: 9.7 ^{o}C Salinity: 32.7 Oxygen Saturation: 89% pH: 8.1
Photoperiod	12-h light per day, 50 Lux.
Positive Control	No
Remarks field for test conditions	Pretreatment: none, fish held for a minimum of 14 days before testing. No feeding 24 hours prior to and during the test. All organisms were observed for mortality twice daily
Results	Cumulative mortality (%) was as follows:

	% Cumulative Mortality (n=21)						
Nominal Concentration (umol/L)	0 hours	48 hours	72 hours	96 hours	120 hours	144 hours	168 hours
0	0	0	0	0	0	0	0
0.5	0	0	5	5	5	5	2

	1 0 0 0 0 0 0 0 2.1 0 0 0 10* 10* 14* 19* 4.2 0 5 67* 100* - - - *=Significantly different from control p≤0.05. The maximum nominal concentration causing no mortality was 1.0 umol/L. The minimum concentration causing 100% mortality was 4.2 umol/L. The 96 hr LC50 was estimated by graphical interpolation to be 2.9 umol/L. No mortality was observed in the vehicle control (methanol/water) group.
Conclusions	The 96 hr LC50 was 2.9 umol/L. The 96 hour NOEC was 1 umol//L.
Data Quality	Reliable with restriction (Klimisch Code). Restriction due to lack of analytical confirmation of test material concentration.
References	Environmental Toxicology and Chemistry, Volume 17, No. 4, 740-746 (1998).
Other	Updated: September 5, 2003

4. Toxicity

4.1 Acute Toxicity

4.1.1 Acute Oral Toxicity

Robust Summary 28-Acute Oral –1

Test Substance	
CAS #	CAS# 72624-02-3
Chemical Name	Phenol, heptyl derivatives
Remarks	100% active ingredient
Method	
Method/Guideline followed	Similar to FHSA 16 CFR 1500.3
Test Type	Acute oral toxicity
GLP (Y/N)	Y
Year (Study Performed)	1982
Species/Strain	Rats/Sprague-Dawley strain
Sex	Male and Female
No. of animals/dose	5/sex
Vehicle	None
Route of administration	Oral (intragastric)
Dose level	2.0 g/kg
Dose volume	Not provided
Control group included	No
Remarks field for test conditions	A single dose of the undiluted test material was administered intragastrically to five fasted (over night) male and female rats. The animals were observed for signs of toxicity or behavioral changes frequently on the day of dosing and twice daily thereafter. Individual weights were recorded on the day of dosing. Gross autopsies were performed on all animals.
Results	LD50 <2.0 g/kg (males and females)
Remarks	Four of five females died within 24 hours post dosing. The remaining female and all of the males died on days 2 and 3. The animals were ruffled after 3 hours. They had dirty oily coats, appeared depressed and had discharge around the mouth and nose after 24 hours. All animals died prior to the first post dosing weighing interval. At necropsy pale and mottled livers and pale spleens were observed.

Conclusions	The test article, when administered as received to male and female Sprague-Dawley rats, had an acute oral LD50 of <2.0 g/kg (males and females.).
Data Quality	Reliable with restriction (Klimisch Code). Restriction due to the lack of individual animal data in the final report.
References	Unpublished confidential business information
Other	Updated: 5/30/2003

Robust Summary 28-Acute Oral –1

Test Substance	
CAS #	CAS# 72624-02-3
Chemical Name	Phenol, heptyl derivatives
Remarks	100% active ingredient
Method	
Method/Guideline followed	Similar to FHSA 16 CFR 1500.3
Test Type	Acute oral toxicity
GLP (Y/N)	Y
Year (Study Performed)	1982
Species/Strain	Rats/Sprague-Dawley strain
Sex	Male and Female
No. of animals/dose	5/sex
Vehicle	None
Route of administration	Oral (intragastric)
Dose level	0.2 g/kg
Dose volume	Not provided
Control group included	No
Remarks field for test conditions	A single dose of the undiluted test material was administered intragastrically to five fasted (over night) male and female rats. The animals were observed for signs of toxicity or behavioral changes frequently on the day of dosing and twice daily thereafter. Individual weights were recorded on the day of dosing, on day 7 and at termination. All animals were euthanized at the conclusion of the observation period. Gross autopsies were performed on all animals after 14 days.
Results	LD50 >0.2 g/kg (males and females)
Remarks	All animals survived the duration of the study. The animals were ruffled after 3 hours. They had dirty coats with urine stains and a bloody discharge around the nose and mouth within 24 hours. Between 12 and 24 hours the animals were vocalizing. The dirty coats and discharge gradually improved and the animals appeared to be recovered by day 3. The males exhibited an 8% decrease in mean body weight during week 1. Male body weights recovered during week 2. Female body weights were unremarkable. Necropsy results were unremarkable.
Conclusions	The test article, when administered as received to male and female Sprague-Dawley rats, had an acute oral LD50 of >0.2 g/kg (males and females.).
Data Quality	Reliable with restriction (Klimisch Code). Restriction due to the lack of individual animal data in the final report.
References	Unpublished confidential business information
Other	Updated: 5/30/2003

4.1.2 Acute Dermal Toxicity

Test Substance	
CAS #	CAS# 72624-02-3
Chemical Name	Phenol, heptyl derivatives
Remarks	100% active ingredient
Method	
Method/Guideline followed	OECD Guideline 402 and EPA Pesticide Assessment Guidelines (November 1982)
Test Type	Acute dermal toxicity (Limit Test)
GLP (Y/N)	Yes
Year (Study Performed)	1985
Species/Strain	Rabbits/New Zealand White
Sex	Male and female
No. of animals/sex/group	5
Vehicle	None
Route of administration	Dermal
Dose level	2 g/kg
Control group included	No
Remarks field for test conditions	Approximately 24 hours prior to topical application of the test material, the hair of each animal was closely clipped. A single dose of 2 g/kg of the undiluted test material was administered dermally to five male and five female animals. The test material was kept in contact with the skin for a period of 24 consecutive hours under a gauze pad and wrapped with an impervious material. The application site was washed clean of residual test material at the end of the 24-hour exposure period. The animals were observed for abnormal clinical signs once or twice/day for 14 days after treatment. Individual body weights were recorded on the day of dosing, weekly thereafter and prior to sacrifice. Gross necropsies were performed on all animals on Day 14.
Results	LD50 > 2.0 g/kg (males and females)
Remarks	No male mortality was observed. One female animal was found dead on day 12. This female exhibited a body weight loss at day 7 as well as diarrhea, signs of dehydration and a lack of formed fecal material in the lower gastrointestinal tract at necropsy. In the males signs of necrosis and severe edema were observed in 5 of 5 animals after unwrapping at 24 hours. Eschar was noted at 48 hours (3/5) and 72 hours (2/5). The eschar began to peel at 7 days. One male exhibited a loss of body weight at 7 and 14 days. In the females signs of necrosis and severe edema were observed in 5 of 5 animals after unwrapping at 24 hours. Eschar was noted at 48 hours (5/5). The eschar began to peel at 8 days. No gross necropsy findings were evident in the males or females that were sacrificed on day 14.

Conclusions	The test article, when administered dermally as received to 5 male and 5 female New Zealand white rabbits had an acute dermal LD50 of greater than 2.0 g/kg.
Data Quality	Reliable without restriction (Klimisch Code).
References	Unpublished confidential business information
Other	Updated: 5/29/2003

4.2 Genetic Toxicity:

Robust Summary 28-Gentox:-1

Test Substance	
CAS #	CAS# 72624-02-3
Chemical Name	Phenol, heptyl derivatives
Remarks	100% active ingredient
Method	
Method/Guideline followed	OECD Guideline 471
Test Type	Bacterial Reverse Mutation Assay
GLP (Y/N)	Y
Year (Study Performed)	1993
Test System	*Salmonella typhimurium* and *Escherichia Coli*
Strains Tested	*Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537; TA1538 *Escherichia Coli* tester strain WP2*uvr*A
Exposure Method	Plate incorporation
Test Substance Doses/concentration levels	Initial assay: All *Salmonella* Strains + (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate All *Salmonella* Strains - (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate WP2*uvr*A + (S9): 0.167, 0.5, 1.67, 5.0, 16.7, and 50 ug/plate WP2*uvr*A - (S9): 0.167, 0.5, 1.67, 5.0, 16.7, and 50 ug/plate Confirmatory Assay A: TA1538 + (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate TA1535, 1537, 98, 100 and WP2*uvr*A + (S9): 1.67, 5.0, 16.7, 50, 167 and 500 ug/plate All *Salmonella* Strains - (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate WP2*uvr*A - (S9): 0.167, 0.5, 1.67, 5.0, 16.7, and 50 ug/plate Confirmatory Assay B: TA1535, 1537, 98 and 100 + (S9): 0.5, 1.67, 5.0, 16.7, 50 and 100 ug/plate WP2*uvr*A + (S9): 0.167, 0.5, 1.67, 5.0, 16.7, 50 and 100ug/plate
Metabolic Activation	With and without (6% S9 fraction mix of livers of Aroclor 1254 pretreated Sprague Dawley rats)
Vehicle	DMSO
Tester strain, activation status, Positive Controls and concentration level	TA98 +S9 2-anthramine 2.5 ug/plate TA98 -S9 2-nitroflourene 5.0 ug/plate TA100 +S9 2-anthramine 2.5 ug/plate TA100 -S9 sodium azide 10.0 ug/plate TA1535 +S9 2-anthramine 2.5 ug/plate TA1535 -S9 sodium azide 10.0 ug/plate TA1537 +S9 2-anthramine 2.5 ug/plate TA1537 -S9 9-aminoacridine 150.0 ug/plate TA1538 +S9 2-anthramine 2.5 ug/plate TA1538 -S9 2-nitroflourene 5.0 ug/plate WP2*uvr*A +S9 2-anthramine 2.5 ug/plate WP2*uvr*A –S9 ENNG 2.0 ug/plate
Vehicle Control	DMSO

Statistical Analysis	Mean revertant colony count and standard deviation were determined for each dose point. Statistical analysis was performed as appropriate.
Dose Rangefinding Study	Conducted using tester strains TA1538, TA100 and WP2*uvr*A and ten doses of test material ranging from 0.5to 5,000 ug/plate, duplicate plates/dose without metabolic activation. Cytotoxicity was evaluated.
S9 Optimization Study	Yes
Remarks field for test conditions	In the main study there were two treatment sets for each tester strain, with (+S9) and without (-S9) metabolic activation. Each of the tester strains was dosed with several concentrations of test substance, vehicle controls, and a positive control. Three plates/dose group/strain/treatment set were evaluated. The results of the initial assay were confirmed in two independent confirmatory experiments. 0.1 mL of test material, positive control or vehicle control were added to each plate along with 0.1 mL of tester strain, S9 mix (if needed) and 2.0 mL of top agar. This was overlaid onto the surface of minimal bottom agar in a petri dish. Plates were incubated for 48 hours at 37^{o}C. The condition of the bacterial background lawn was evaluated for cytotoxicity and test article precipitate. Revertant colonies were counted using an electronic colony counter. A positive result was defined as a statistically significant dose dependent increase in the number of revertants with at least one dose level inducing a revertant frequency that is two-fold the level of the solvent control.
Results	The test substance was not mutagenic in this assay with or without metabolic activation.
Remarks	The test material was evaluated in a toxicity prescreen in strains TA1538, TA100 and WP2*uvr*A. Results of this evaluation indicated that the test material produced inhibited growth or complete toxicity in all three tester strains at all dose levels tested (50-5000 ug/plate). The dose range find study was repeated at doses ranging from 0.5 to 167 ug/plate. Doses > 5 ug/plate were toxic in TA1538 and TA100 and in doses > 16.7 ug/plate in WP2*uvr*A. Based on these results the mutagenicity assay was conducted at the concentrations listed above. The test material was soluble at all concentrations tested. In the mutagenicity study, inhibited growth was observed in all tester strains at doses between 0.5 and 16.7 and/or 50 ug/plate with S9, and in TA1538 at 5 and 16.7 ug/plate without S9. Revertant frequencies at all dose levels in all tester strains with and without metabolic activation were less than those observed in the concurrent negative controls. The test material was re-evaluated in a confirmatory assay in all tester strains activation at the confirmatory dose levels listed above (Confirmatory Assay A). The test material was soluble at all concentrations tested. Inhibited growth was observed in all tester strains at the highest two or three concentrations tested with and without metabolic activation. Revertant frequencies at all five dose levels in all *Salmonella* tester strains with metabolic activation, and in all six tester strains without activation, approximated or were less than those observed in the concurrent negative controls. A statistically significant, 2.6 fold increase was observed in the revertant frequency of WP2*uvr*A at 1.67 ug/plate. This increase was not dose related. **Based on these confirmatory assay results a second confirmatory assay** (Confirmatory Assay B) was conducted. The test article was freely soluble and inhibited growth was observed in all tester strains at 16.7 and 50 and/or 100 ug/plate with activation. A statistically significant, 2.1 fold increase was observed in the revertant frequency of TA1537 at 16.7 ug/plate. This increase was not dose related. The Study Director considered the slight increases observed in the revertant frequencies of TA1537 and

	WP2*uvr*A to be random fluctuations of the revertant frequencies. The positive and negative controls for each respective test strain were within acceptable limits.
Conclusions	Under the conditions of this study, the test material was not mutagenic.
Data Quality	Reliable without restriction (Klimisch Code)
References	Unpublished confidential business information
Other	Updated: 7/17/2003

5.8